Determinants of postoperative atrial fibrillation in patients undergoing coronary artery bypass grafting: prophylactic beta-blocker plus statin therapy for prevention of postoperative atrial fibrillation

Koroner bypass cerrahisi uygulanan hastalarda ameliyat sonrası atriyal fibrilasyonun belirleyicileri: Ameliyat sonrası atriyal fibrilasyonun önlenmesinde profilaktik beta-bloker ve statin tedavisi

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Background: The aim of this study was to determine the incidence and predictors of post-coronary artery bypass grafting (CABG) atrial fibrillation (AF) and also, to investigate the effect of β-blocker plus statin use on post-CABG AF.

Methods: Between September 2003 and April 2004, 121 consecutive patients (99 males, 22 females; mean age 61.2±7.5 years; range 39 to 78 years) undergoing elective CABG surgery were included to the study. The patients were divided into two groups according to the absence [group-SR (sinus ryhtym), n=92] or presence [group-AF, n=29] of post-CABG AF. Variables were compared by Fischer's exact test, chi-square and independent samples t-test. Multivariate logistic regression analysis was used for independent predictors of post-CABG AF.

Results: Post-CABG AF was detected in 23.9%. Mean age (66.6±7.2 vs 59.4±7.9, p=0.0001) and the incidence of chronic obstructive pulmonary disease (13.8 vs 2.2%, p=0.012) were higher in group-AF. The patient is older than 63 years of age (41.3 vs 13.3%, p=0.0001, area under the ROC curve of 0.748) have an increased prevalance of post-CABG AF. Much more frequent occurrence of post-CABG AF was in the patients without using β-blocker drug (40% vs 19.8%, p=0.035). Post-CABG AF was lower in the patients receiving statin than the patients not receiving statin (15.9% vs 34.6%, p=0.017). Post-CABG AF was lower in the patients receiving β-blocker plus statin therapy (13.3 vs 43.8%, p=0.015) than the patients not receiving these drugs. White blood cell (WBC) count of the patients receiving statin were lower than the patients not receiving statin (10618±3540 vs 13038±5661, p=0.005) in postoperative day 2 (POD 2). Chest tube drainage (1048.6±776.2 vs 641.5±514.6, p=0.001), and WBC count (13210±5550 vs 11160±4320, p=0.041), serum BUN (33.8±32.5 vs 21.6±13, p=0.004) in POD 2 were higher in group-AF. Intensive care unit stay (69.8±47.1 vs 53.6±19.2, p=0.008) and lenght of stay (LOS>7 days, 58.6 vs 37%, p=0.039) were higher in group-AF. Advanced age (OR=1.099, p=0.018) and increased postoperative drainage (OR=1.001, p=0.045) were independent predictors of post-CABG AF.

Conclusions: Age and postoperative blood loss are independent predictors of post-CABG AF. β-blocker plus statin therapy seems to be the best medication of choice on reducing the incidence of post-CABG AF. However, new prospective studies about the efficacy of this combination therapy are required.

Key words: Adrenergic beta-antagonists; atrial fibrillation/etiology; coronary artery bypass.

Amaç: Bu çalışmada koroner arter bypass greftleme (KABG) sonrası atriyal fibrilasyon (AF) insidansı ve belirleyicileri ile β-bloker ve statin kullanımının AF oluşumu üzerine etkinliğinin araştırılması amaçlandı.

Çalışma planı: Eylül 2003 ve Nisan 2004 tarihleri arasında ardışık olarak KABG cerrahisi uygulanan 121 hasta (99 kadın, 22 erkek; ort. yaş 61.2±7.5; dağılım 39-78) çalışmaya alındı. Hastalar, KABG sonrası AF varlığı [grup-AF, n=29] ya da yokluğuna [grup-SR (sinus), n=92] göre iki gruba ayrıldı. Değişkenler, Fischer's exact test, chi-square ve independent samples t-test ile kıyaslandı. Koroner arter bypass greftleme sonrası AF'nin bağımsız belirleyicilerini saptamak için multivaryans lojistik regresyon analizi yapıldı.

Bulgular: Hastaların %23.9'unda KABG sonrası AF saptandı. Ortalama yaş (66.6±7.2 ve 59.4±7.9, p=0.0001) ve kronik obstrüktif akciğer hastalığı insidansı (%13.8 ve %2.2, p=0.012) grup-AF'de daha yüksekti. Altmış üç yaşından daha büyük olan hastalarda KABG sonrası AF anlamlı olarak daha yüksek prevalansa sahipti (%41.3 ve %13.3, p=0.0001, ROC eğrisi altında kalan alan = 0.748). β-bloker kullanmayan hastalarda AF sıklığı daha fazlaydı (%40 ve %19.8, p=0.035). Statin alan hastalarda AF, almayan hastalara oranla daha düşük oranlardaydı (%15.9 ve %34.6, p=0.017). β-bloker ve statini birlikte alan hastalarda, bu iki ilacı da almayan hastalara göre AF oldukça düşük oranda saptandı (%13.3 ve %43.8, p=0.015). Statin alan hastalarda, statin almayan hastalara oranla ameliyat sonrası ikinci gündeki lökosit sayısı (10618±3540 ve 13038±5661, p=0.005) daha düşüktü. Mediastinal drenaj (1048.6±776.2 ve 641.5±514.6, p=0.001), ameliyat sonrası ikinci gündeki lökosit sayısı (13210±5550 ve 11160±4320, p=0.041) ve serum BUN (33.8±32.5 ve 21.6±13, p=0.004) değerleri grup-AF'de daha yüksekti. Yoğun bakımda (69.8±47.1 saat ve 53.6±19.2 saat, p=0.008) ve hastanede kalış süresi (LOS >7 gün, %58.6 ve %37, p=0.039) grup-AF'de anlamlı olarak daha yüksek bulundu. İleri yaş (OR=1.099, p=0.018) ve ameliyat sonrası drenaj miktarı (OR=1.001, p=0.045) KABG sonrası AF için bağımsız belirleyiciler olarak saptandı.

Sonuç: Yaş ve ameliyat sonrası drenaj KABG sonrası AF için bağımsız belirleyicilerdir. β-bloker ve statinin birlikte kullanılması AF insidansını azaltan en iyi tedavi seçeneği gibi görünmektedir. Ancak, bu kombinasyon tedavisinin etkinliğini araştıran yeni prospektif çalışmalara ihtiyaç vardır.

Anahtar sözcükler: Adrenerjik beta antagonist; atriyal fibrilasyon/etyoloji; koroner bypass.

Received: March 28, 2005 *Accepted:* September 21, 2005

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Atrial fibrillation (AF) is the disturbance of cardiac ryhthm that is considered to be the result of multiple small reentrant circuits that cause numerous circulating excitation wavefronts within the myocardium. The consequences of AF for the patient include the loss of atrial transport, an irregular and poorly controlled ventricular rate, a reduction in cardiac output, symptoms of palpitations, dizziness, and dyspnea, and an increased risk of thromboembolism and stroke.[1]

Atrial fibrillation is the most frequently encountered arrhythmic complication following coronary artery bypass grafting (CABG) surgery which incurs significant cost to the health care system because of the increased length of intensive care unit and hospital stay.[2] The incidence of post-CABG AF has been reported to be substantial, ranging from 10 to 40% in various studies. Post-CABG AF most often develops between second and fifth day, with a peak incidence in the first 2 to 3 days after the operation.[2,3] Although anesthetic regimes, surgical techniques, myocardial protection, cardiopulmonary bypass and care of the patients in intensive care unit improve in CABG surgery, the incidence of post-CABG AF has not changed and it may even increase with the aging patient population. Off-pump surgery reduces the incidence of post-CABG AF but not eliminates.[4]

Despite post-CABG AF is often regarded as transient, benign and well-tolerated condition, it may lead to severe life-threatening complications such as significant hemodynamic instability and thromboembolic events with mortal sequela.[4,5] A pathophysiological mechanism responsible for post-CABG AF is still unknown, and is most likely multifactorial. An advanced age, male sex, preoperative β-blockers withdrawal, chronic obstructive pulmonary disease, longer aortic cross-clamp time, increased postoperative sympathetic activation, prolonged P-wave duration, increased preoperative atrial effective refractory period (AERP) dispersion, inflammation and atrial structural changes, left atrial enlargement, atrial ischemia, severe coronary artery disease, an obstructive disease of the sino-atrial and atrioventricular nodal arteries play a role in occurrence of post-CABG AF.[2,6-11]

Prophylactic β-blocker therapy is clearly effective in reducing the incidence and the number of episodes of post CABG AF.[1] Statins (hydroxymethylglutaryl coenzyme A [HMG-CoA] reductase inhibitors) are known as lipid-lowering agents; also have antioxidative, antiinflammatory and CRP-lowering effects.[9] A recent study has demonstrated that statin therapy reduces the incidence of atrial fibrillation in patients with coronary heart disease independent of its lipid-lowering effects.[12] The aim of this study was to define the incidence and determinants of post-CABG AF and the effect of β-blocker plus statin use on preventing and reducing of post-CABG AF.

PATIENTS AND METHODS

Patients selection protocol. Between September 2003 and April 2004, 121 consecutive patients (99 males, 22 females; mean age 61.2±7.5 years; range 39 to 78 years) undergoing elective CABG surgery were included to the study. Patients with previous history of rhythm disturbance, concomitant operations such as annuloplasty, valve replacement or aneurysmectomy were excluded from the study. The patients were divided into two groups according to the absence (n=92, group-SR, group of sinus ryhthm) or presence (n=29, group-AF, group of postoperative atrial fibrillation) of post-CABG AF.

Patient characteristics and variables. Demographic data collected for each patient included age, sex, hypertension, diabetes mellitus, chronic obstructive pulmonary disease (COPD), smoking, preoperative cardiac status and medications, left ventricle (LV) ejection fraction, left main coronary artery (LMCA) disease, associated valvular heart disease, peripheric arterial occlusive disease (PAOD), previous cerebrovascular accident (CVA). Also operative and postoperative data recorded for each patients included number of distal anastomosis, X-clamp time, cardiopulmonary bypass (CPB) time, extubation time, mean blood pressure during ICU, total drainage amount, CBC and serum BUN value in postoperative day 2 (POD 2), stay in ICU (including ICU readmission), lenght of stay (>7 days) [LOS].

Cardiac rhythm evaluation and diagnosis of post-CABG AF. Heart rate and ECG lead II were continuously monitored in intensive care unit. Post-CABG AF was defined by the documentation of AF any duration at any time in the postoperative period on a physician assessment, on the basis of a rhythm strip or 12-lead electrocardiogram (ECG) recording. The diagnosis of AF was established by an irregular random ventricular rate without vissible P waves on 12-lead ECG.

Anesthesia. In all groups, anesthesia was induced with a continuous infusion of remifentanil (Ultiva® GlaxoSmithKline) at 0.2 µg.kg-1.min-1 and propofol (Diprivan® AstraZeneca) at 150-200 mg. Anesthesia was maintained with 0.2–0.4 µg.kg-1.min-1 remifentanil and desflurane (Suprane® Baxter) (3%-4% end-expiratory concentration). Controlled mechanical ventilation with 50% oxygen in air was provided to achieve normocapnia as indicated by continuous end-tidal CO_2 monitoring and intermittent arterial blood gas studies. Muscle relaxation was obtained with 0.1 mg/kg vecuronium (Norcuron® Organon).

Surgical techniques and anticoagulation protocol. For all of the patients, median sternotomy incision was performed first and then IMA was harvested according to the pedunculated technique. When the IMA harvesting was completed, pericardium was opened and heparin (300 U/kg) was administered. Heparin dosage was adjusted according to an activated coagulation time (ACT) level. Supplemental doses of heparin were administered to maintain ACT of greater than 480 seconds. All the CABG operation was performed on cardiopulmonary bypass. The distal anastomoses were done during a single period of total aortic occlusion, whereas the proximal ones were performed after removal of the total occluding clamp.

Cardiopulmonary bypass and myocardial protection. CPB was established in standard manner. Aortic cannulation (24F) and two-stage venous cannulation was performed for CPB. A roller pump, membrane oxygenator and pulsatile flow were used, flow rate was 2.4 l/m^2/min. Moderate hypothermia (28 °C) was employed. Intermittent antegrade cold (4 °C) blood cardioplegia (4/1 ratio) was used in every 20 minutes. Topical cooling was also used for myocardial protection. Terminal warm blood cardioplegia was used routinely for all the patients. Arterial blood pressure was kept in range of 60-80 mmHg during CPB. After the termination of CPB and administration of protamin, ACT was maintained between 100 and 120 seconds.

Postoperative protocols. Postoperative ventilation protocol were as following; SIMV (12-14/min.), tidal volume of 8 ml/kg, PEEP 5-10 cm H_2O, I/E ratio of 1/2. Arterial blood sample were taken for blood gases analysis in every one hour in entubated patients to adjust ventilation rate and keep the arterial pH between 7.35 and 7.45. Extubation was accomplished when the patient was haemodynamically stable and alert and able to maintain adequate blood gases during a short trial on pressure support ventilation of 5 cmH_2O. Invasive/noninvasive blood pressure, central venous pressure, heart rate, ECG, oxygen saturation, temperature, chest tube drainage and urine output were continuously monitored in intensive care unit. Potassium, calcium, sodium and magnesium suplements were provided as necessary to maintain electrolytic balance within the normal range. An inotropic support and intra aortic balloon pump, if indicated, were provided in order to achieve stable haemodynamic condition. Preoperative β-blockers were continued postoperatively to avoid withdrawal.

Statistical analysis. SPSS (SPSS for windows, version 10.0, SPSS Inc, Chicago) was used for statistical analysis. Data are reported as a mean±SD or as a percent. Variables regarding preoperative, intraoperative and postoperative parameters between groups were compared by using Fischer's exact test, chi-square and independent samples t test. A P-value of less than 0.05 was considered statistically significant. Univariate factors exhibiting a P-value of less than 0.035 were entered into multivariate logistic regression analysis in order to assess the independent correlates for post-CABG AF. Again, statistical significance was obtained only for P-value of less than 0.05. Recevier-operator characteristic (ROC) curve analysis was used for determining cut off value of age as a predictor of post-CABG AF.

RESULTS

Mean age (66.68±7.2 vs 59.47±7.92, p=0.0001) and the incidence of COPD (13.8% vs 2.2%, p=0.012) were higher in group-AF than group-SR (Table 1). Post-CABG AF was detected in 23.9% of the patients. The patient is older than 63 years of age (41.3 vs 13.3%, p=0.0001, area under the ROC curve of 0.748) have an increased prevalance of post-CABG AF. Much more frequent occurrence of post-CABG AF was noticed in the patients without using β-blocker drug (40% vs 19.8%, p=0.035). Post-CABG AF was lower in the patients receiving statin than the patients not receiving statin (15.9% vs 34.6%, p=0.017). Post-CABG AF was lower in the patients receiving β-blocker plus statin than the patients not receiving these drugs (13.3% vs 43.8%, p=0.015) (Table 2). White blood cell count in POD 2 were lower in the patients receiving statin than the patients not receiving statin (10618±3540 vs 13038±5661, p=0.005) (Table 3). There were no differences between the groups regarding operative parameters (Table 1). Postoperative bleeding (1048.62±776.28 vs 641.57±514.65, p=0.001), WBC count in POD 2 (13210±5550 vs 11160±4320, p=0.041), serum BUN in POD 2 (33.8±32.5 vs 21.67±13, p=0.004) were higher in group-AF than group-SR. Intensive care unit stay (69.86±47.16 vs 53.60±19.20, p=0.008) and LOS [>7 days] (58.6% vs 37%, p=0.039) were higher in group-AF than group-SR (Table 4). Mortality rate were similar in both groups (3.2% versus 3.4%, p>0.05).

The COPD patients with post CABG AF had lower FEV1 value (1.68±0.3) than the other COPD patients without post CABG AF. Prolonged ventilation was needed in one of them and re-intubation in postoperative day 2 was done in the other.

Multivariate logistic regression analysis identified an advanced age and increased postoperative drainage to be independent predictors of post-CABG AF. The OR and the P-value for each multivariate predictor are shown in table 5.

DISCUSSION

Introducing new, modern surgical tecniques and cardiac protection methods made the cardiac surgeons more desirous in performing CABG surgery in elderly patients with high risk. This tendency results in increased postoperative rhythm disturbance such as post-CABG AF. The incidence of post-CABG AF has been reported to be substantial, ranging from 10 to 40% in various studies.[2,3] In our study, post-CABG AF was detected in 23.9% of the patients. We found that post-CABG AF is associated with a longer stay in the intensive care unit (69.86±47.16 vs 53.60±19.20, p=0.008) and length of hospital stay (LOS>7 days, 58.6% vs 37%, p=0.039) resulting in higher costs.

A pathophysiological mechanism of post-CABG AF is still unknown. Many factors related to the occurrence of post-CABG AF have been documented. The most reliable predictors were patient's age and preoperative β-blockers withdrawal.[2,13,14] However, some authors underlined the importance of other variables, such as the left atrial enlargement and severe coronary artery disease, atrial structural changes, atrial ischemia, an obstructive disease of the sino-atrial and atrioventricular nodal arteries, right coronary artery stenosis, an increased P-wave duration, increased preoperative AERP dispersion, longer aortic cross-clamp time, postoperative fluid and electrolytes shifts, sympathetic hyperactivation, an increased postoperative drainage and inflammation.[2,7,9-11,15-17] Age-related structural changes, such as increased atrial fibrosis and atrial dilation, might explain the increased incidence of post-CABG AF in old patients.[18] It is well known that aging causes degenerative changes in the atrial myocardium that lead to alterations in electrical properties of the SA and AV nodes and atria, which contribute to fragmentation of the propagating impulse.[19] In our study, an advanced age (p=0.018) and increased postoperative drainage (p=0.045) were independent predictors of post-CABG AF, and an age greater than 63 years was the strongest predictor of post-CABG AF (41.3% in age<63 vs 13.3% in age≥, p=0.0001, area under the ROC curve of 0.748). Age is not a changeable factor, but the strategies reducing postoperative drainage such as minimal dissection, a meticulous haemostatic control, the use of heparin-bounded circuits, and the use of antifibrinolytic drugs reduce the incidence of post-CABG AF and as a consequence, improve postoperative course of the patients.

The association of COPD and an increased incidence of post-CABG AF is well established.[20,21] We found that the incidence of COPD were higher in group-AF than group-SR (13.8% vs 2.2%, p=0.012). The occurrence of post-CABG AF is attributable to several factors such as hypoxemia, hypercapnia and medications for COPD (methylxantine and β2 mimetics therapy).[20] There is strong relation between FEV1 and post-CABG AF. Preoperative FEV1 value is known as major predetermining factors of mortality, morbidity

Table 1. Preoperative patient's characteristics and operative parameters

Parameters	Group-SR (n=92)	Group-AF (n=29)	*p* value
Age	59.47±7.92	66.68±7.2	0.0001*
Sex (Male/female)	73/19	26/3	0.216
Hypertension	38	17	0.102
Diabetes mellitus	29	10	0.766
COPD	2 (2.2%)	4(13.8%)	0.012*
Smoking	51	7	0.197
Anginal status			0.643
Unstable	8	1	–
Stable	60	20	–
No angina	24	8	–
Previous MI (+/-)	39/53	14/15	0.416
LV ejection fraction	51.64±9.27	50.65±7.82	0.604
LMCA disease	6	2	0.961
Associated valvular heart disease	8	5	0.195
PAOD	5	1	0.667
Previous CVA	1	0	0.573
No. of distal anastomosis	3.22±1.02	3.20±0.94	0.921
X-clamp time	75.2±30.4	83.4±31.6	0.11
Total CPB time	105.9±35.8	110.4±37.6	0.16

COPD: Chronic obstructive pulmonary disease; CVA: Cerebrovascular accident; LMCA: Left main coronary artery; LV: Left ventricle; MI: Myocard infarction; PAOD: Peripheric arterial occlusive disease; X-clamp: Cross clamp.

Table 2. Patient's medication

Drug	Number of patients	Post-CABG AF		*p* value
		n	%	
β-blocker				
• +	96	19	19.8	0.035*
• –	25	10	40	
ACE inhibitors				
• +	77	19	24.7	0.809
• –	44	10	22.7	
Ca^{++} channel blockers				
• +	17	6	35.3	0.238
• –	104	23	22.1	
Digoxin				
• +	3	1	33.3	0.564
• –	118	28	23.7	
Diuretics				
• +	18	6	33.3	0.313
• –	103	23	22.3	
Statin				
• +	69	11	15.9	0.017*
• –	52	18	34.6	
ASA				
• +	97	23	23.7	0.895
• –	24	6	25	
Clopidogrel				
• +	8	1	12.5	0.678
• –	113	28	24.8	
β-blocker plus statin				
• +	60	8	13.3	0.015*
• – (ϕ)	16	7	43.8	

(ϕ): Indicates neither β-blocker nor statin use.

and supraventricular tachyarrhythmias (atrial fibrillation, atrial flutter, multifocal atrial tachycardia) after CABG in patients with COPD. Hypoxemia is a predominant mechanism in occurrence of post CABG AF.[20] In our study, the COPD patients with post-CABG AF had lower FEV1 value (1.68±0.3) than the other COPD patients without post-CABG AF. Prolonged ventilation was needed in one of them and re-intubation in postoperative day 2 was done in the other.

The hyperadrenergic state of the heart in early postoperative period is one of the factors related to the occurrence of post-CABG AF. CABG surgery has been known to significantly increase epinephrine and norepinephrine levels, and these abnormal levels may persist for up to 3 postoperative days. The presence of a hyperadrenergic state may explain why β-blocker drugs are effective in preventing and controlling of post-CABG AF in some individuals. Prevention of post-CABG AF is the most desirable course for management. Prophylactic β-blocker therapy, starting preoperatively and continuing postoperatively, is clearly helpful in reducing the incidence and the number of episodes of post-CABG AF. It is clear from the research on prevention of post-CABG AF that β-blocker agents are the most effective means of prevention. β-blocking agents reduce catecholamine secretion, depress AV node con-

Table 3. Relationship between statin use and white blood cell count in postoperative day 2 (WBC count in POD 2)

Drug	Number of patients	WBC count in POD2	*p* value
Statin use	69	10618±3540	0.005*
No statin use	52	13038±5661	

Table 4. Postoperative parameters

Parameters	Group-SR	Group-AF	*p* value
Extubation time	7.79±3.1	8.76±4.22	0.598
Mean blood pressure in ICU	117.39±12.12	120.51±16.54	0.272
Total drainage	641.57±514.65	1048.62±776.28	0.001*
CBC in POD 2			
Hemoglobin	11.15±1.23	10.52±1.09	0.015*
Hct	32.89±3.79	30.84±3.7	0.012*
White blood cell	11160±4320	13210±5550	0.041*
Serum BUN in POD 2	21.67±13	33.8±32.5	0.004*
Stay in ICU (including readmission)	53.60±19.20 h	69.86±47.16 h	0.008*
LOS (>7 days)	34 (37%)	17 (58.6%)	0.039*

ICU: Intensive care unit; LOS: Length of stay; POD2: Postoperative day 2.

duction, and reduce myocardial ischemia.[1] In our study, post-CABG AF was significantly lower in the patients receiving β-blockers than the patients not receiving these drugs (19.8% vs 40%, p=0.035).

Cardiac surgery triggers an inflammatory response that includes the activation of the complement system and the release of inflammatory mediators.[22,23] White blood cell count, an inexpensive and readily available marker of systemic inflammation, usually peaks after 36 to 60 hours in patients who undergo on-pump surgery, which coincides with the time course for the occurrence of post-CABG AF.[23,24] Our study showed that postoperative WBC counts in POD 2 (13210±5550 vs 11160±4320, p=0.041) were significantly greater in patients with post-CABG AF. The complement system is activated and proinflammatory cytokines is released during and after cardiac surgery. Bruins et al.[22] reported a biphasic activation of the complement system after cardiac surgery, with the second phase involving CRP. Acutely, complement activation during CPB occurs from the contact of blood with the extracorporeal circuits, as well as by the formation of heparin-protamine complexes. A second phase then occurs, with an increase in CRP, peaking on the second postoperative day, and increases complement-CRP complexes, peaking on the second on third postoperative day.[22] The incidence of post-CABG AF similary peaks at these times. The present study, showing a strong association between WBC count elevation and the occurence of post-CABG AF supports a role for inflammation in the pathogenesis of post-CABG AF. Aside from lipids-lowering effect, statins have been shown to have other effects such as improvement of endothelial function, reduced oxidative stress, antiinflammatory and antithrombotic properties, CRP-lowering effect, and anti-arrhythmogenic effect.[9] A recent study has demostrated that statin therapy reduces the incidence of atrial fibrillation in patients with coronary heart disease independent of its lipid-lowering effects.[12] In our study, we found that post-CABG AF was lower in the patients receiving statin than the patients not receiving statin (15.9% vs 34.6%, p=0.017) and also, statin was significantly reduced postoperative WBC count (10618±3540 vs 13038±5661, p=0.005), and reduced postoperative inflammation.

Although numerous potential postoperative factors have been identified, one potential factor is atrial mechanical remodeling. In the postoperative period it is quite possible that mechanical stretch injury of atrial tissue results in post-CABG AF. Although cardiac dysrhythmias have been traditionally viewed as electrical disorders of the heart, recent evidence has supported the possibility of mechanical or stretch-mediated dysrhythmias.[25] The term for this mechanically induced change in electrophysilogy is mechanoelectrical feedback. This injury can be induced by acute stretch or chronic stretch of atria or ventricules.[25] Through a similar mechanism, an abrupt increase in afterload can have a similar effect.[1] Preoperative left atrial enlargement and elevated atrial pressures have been associated with an increased risk of post-CABG AF.[26-29] In early postoperative period, the clinical conditions increasing postoperative BUN level such as renal and/or cardiac dysfunction result in volume overload. These may cause acute stretch injury in the susceptible atrial myocardium, resulting in electrophysiologic changes that trigger post-CABG AF. In our study, higher BUN values were

Table 5. Multivariate predictors of post-CABG AF

Parameters	The odd ratio	*p* value
Age	1.099	0.018*
β-Blocker	0.599	0.400
Statin	0.450	0.119
Chest tube drainage	1.001	0.045*
Hemoglobin	0.780	0.294
Serum BUN	1.013	0.377

associated with increased risk of post-CABG AF (33.8±32.5 vs 21.67±13, p=0.004).

We suggested that atrial fibrosis, inflammation, ischemia, and acute or chronic atrial stretching frequently contribute to the development of post-CABG AF.

Study limitations

1. WBC was used only as a marker of postoperative inflammation in our study. If hsCRP, IL-6, IL-1β, TNFα, complement (C3,C4,C9) could be used as an inflammatory marker, results would be concluded better.

2. New prospective studies are required in order to define;

- The relation between inflammation and the occurrence of atrial fibrillation after on-pump CABG surgery.

- An efficient cause of statin on reducing of post-CABG inflammation.

- The type, dosage and duration of preoperative usage of statin on prevention of post-CABG atrial fibrillation.

3. Atrial stretching may trigger the occurrence of post-CABG AF. But, further studies are required for refining this issue.

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